REMARKS

Claims 1, 6-9 and 11-26 are currently pending in the application. Claims 1, 6-8, 11 and 15-16 are amended. Claims 2-5 and 10 are canceled. Claims 19-26 are newly added. The amendments find support in the specification and are discussed in the relevant sections below. No new matter is added.

Claim Rejections- 35 USC 102

Claims 1-2, 5, 7-8 and 10-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Bauer et al. (U.S. Patent No. 5, 789,166).

The Office Action states asserts that Bauer et al teach a method for preparing a nucleic acid sample for an analytical procedure, said method comprising treating said sample with a substance that cleaves said template nucleic acid without substantially cleaving said synthetic nucleic acid, and refers to columns 9 and 10 of '166.

Applicant traverses said application on the grounds that Bauer et al. does not teach each and every limitation recited in claim 1 and its dependent claims 7-8 and 11-17, specifically the recited limitation of "a method of preparing a nucleic acid sample for an analytical procedure". Applicant notes that Bauer et al. teaches a method of mutagenesis of a template in a linear amplification mutagenesis reaction, wherein said method comprises a digestion step in which the parental template strands are digested (see column 9, lines 1-20), but Bauer et al. does not teach preparing the sample for an analytical procedure.

Applicant's specification defines the phrase "analytical procedure" in paragraph 23 as a technique which permits determination of one or more of its molecular mass, molecular weight, molecular size, purity length, molecular sequence and/or concentration. Bauer's method of mutagenesis does not prepare a nucleic acid sample for an analytical procedure as defined by Applicant because Bauer et al teaches the formation of double-stranded mutagenized circular DNA after the digestion step, which is then transformed into host microorganisms (see column 11, lines 1-31).

While not acquiescing to the rejections of record, and in order to more fully distinguish Applicant's claimed invention, claim 1 has been amended so that it incorporates the additional step of "subjecting said treated sample to an analytical procedure", as recited in claim 2, and so

that it incorporates the analytical procedures recited in claim 3. Applicant notes that claim 3, which depends directly from claim 1, was not included in this rejection, and thus is not anticipated by Bauer et al. Therefore, Applicant contends that claim 1, as amended, is not anticipated by Bauer et al, and accordingly, that rejected claims 7, 8, and 11-17, which depend on newly amended claim 1, are also not anticipated by Bauer et al. As described below, Claims 2, 5 and 10 have been canceled without prejudice, solely for the purposes of advancing prosecution. For the reasons described above, and in view of the claim amendments, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-3, 5, 7-8 and 10-17 are rejected under 35 USC 102(e) as being anticipated by Yuan (U.S. Patent No. 6,376,210).

The Office Action asserts that in columns 56-57, Yuan teaches a method of preparing a nucleic acid sample for DNA sequencing following amplification comprising treating said sample with a substance that cleaves the template nucleic acid without substantially cleaving the synthetic nucleic acid, and that the substance can be Dpn I.

Applicant notes that Yuan teaches a PCR based method of mutagenesis of a template using the ExSite PCR-based Site Directed Mutagenesis kit in which the resulting mixture of template and newly synthesized DNA is treated with the restriction enzyme Dpn I and with Pfu polymerase, ligated and cloned and sequenced(see columns 56-57).

Applicant traverses the rejection of claim 13, on the grounds that Yuan does not teach each and every limitation recited in claim 13, specifically the recited limitation that "said restriction enzyme specifically cleaves nucleic acid comprising un-modified residues, without substantially cleaving modified residues". Applicant notes that in the PCR based method of mutagenesis, Yuan teaches that "Dpn I digests the in vivo methylated parental template" (see column 56, lines 40-50). However, Applicant notes that Yuan does not teach a method wherein the unmodified newly synthesized DNA is "not substantially cleaved" as required by the claim 13. Therefore, Applicant contends that the limitation that "said restriction enzyme specifically cleaves nucleic acid comprising un-modified residues, without substantially cleaving modified residues" required by Claim 13, is not anticipated by Yuan.

Applicant also traverses the rejection of claim 15, and dependent claim 17 on the grounds that '210 does not teach each and every limitation recited in claims 15 and 17, specifically the recited limitation that "said template nucleic acid is a double stranded nucleic acid", as required by Claims 15 and 17. Applicant notes that Yuan does not specify that the "template nucleic acid is a double stranded nucleic acid" as required by Claims 15 and 17, nor does Yuan teach that "said double stranded template is produced in cells which incorporate methylated adenine residues into DNA molecules during replication", as required by claim 17. Accordingly, Applicant contends that Claims 15 and 17 are not anticipated by Yuan.

As described above, Claim 2 has been cancelled, and claim 1 has been amended so that it incorporates the additional step of "subjecting said treated sample to an analytical procedure", as recited in now canceled claim 2. Further, and solely for the purposes of advancing prosecution, Claim 1 has been amended so that said analytical procedures to which the treated sample is subjected, is one of the analytical procedures recited in claim 3, with the exception of the analytical procedure of DNA sequencing. And Claim 3 has been canceled.

Therefore, Yuan et al, which teaches a method of preparing a nucleic acid sample for the analytical procedure of sequencing the synthetic DNA, following amplification comprising treating said sample with a substance that cleaves the template nucleic acid without substantially cleaving the synthetic nucleic acid, does not anticipate newly amended claim 1 or its dependent claims 7 to 8, and 9 through 17, because Yuan et al. does not teach a method comprising subjecting said treated sample to the recited analytical procedures of gel electrophoresis, anion-exchange chromatography, size-exclusion chromatography, pulse-field electrophoresis, polyacrylamide gel electrophoresis, sieving gel electrophoresis, Northern analysis, or Southern analysis, as required by newly amended Claim 1 and its dependent claims. Applicant notes that claims 5 and 10 have also been canceled without prejudice, as described below. For the reasons described above, and in view of the claim amendments, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-3, 5-9 and 11-17 are rejected under 35 USC 102(e) as being anticipated by Carmichael (U.S. Patent No. **6,376,210**).

Since U.S. Patent No. **6,376,210** was cited in the above reference by Yuan et al., and because U.S. Patent No. **6, 265,167** by Carmichael was listed on Form 892 entitled "Notice of References Cited", Applicant assumes that the 102(e) rejection is over Carmichael (U.S. Patent No. **6, 265,167**). Clarification is respectfully requested.

Applicant traverses the rejection on the grounds that Carmichael et al. does not teach each and every limitation of claim 1 and its dependent claims, specifically the limitation of "wherein said template and said synthetic nucleic acid comprise DNA".

The Office Action states that Carmichael et al. ('167) teaches a transcription reaction wherein a nucleic acid sample is generated, comprising template and synthetic RNA, the improvement being whereby after the transcription reaction and immediately prior to the analysis of the RNA sample, said nucleic acid sample is treated with a substance that cleaves said template nucleic acid and does not substantially cleave the RNA.

As described by the office action, the synthetic nucleic acid taught by Carmichael et al. is clearly RNA, and not DNA as required by the instant claims. Therefore, Carmichael et al. does not anticipate claim 1 and its dependent claims 11 through 17.

Applicant further notes that Carmichael et al. does not teach the limitation recited in claim 17, that "the double stranded template is produced in cells which incorporate methylated adenine residues into DNA molecules during replication". Applicant notes that Example 4 teaches that "clones used to generate RNA probes" were used as templates in an in vitro transcription reaction, (see column 8, line 10), but does not teach what cells the template was produced in. Since Carmichael et al does not teach what cells the template was produced in, the referenced patent by Carmichael et al. does not anticipate the invention as recited in claim 17, comprising the limitation that the double stranded template is produced in cells which incorporate methylated adenine residues into DNA molecules during replication.

Applicant further traverses the rejection on the grounds that Carmichael et al. does not teach each and every limitation recited in claims 11-14, specifically a method comprising "treating said sample with a substance that cleaves the template nucleic acid without substantially cleaving the synthetic nucleic acid", " wherein said substance is a restriction enzyme".

Applicant notes that Carmichael et al further teaches in Example 4 that "following in vitro transcription using T3 or T7 RNA polymerase and [α-^{32}P]UTP, DNA templates were removed by RQ1 DNAse digestion ....". Applicant also notes that DNAse is not a restriction enzyme, and therefore, Carmichael et al. does not teach the digestion of the DNA template with a restriction endonuclease. Accordingly, Applicant contends that Carmichael et al does not teach each and every limitation recited in claims 11-14, and consequently is not anticipatory.

For the sole purpose of more clearly defining Applicant's invention, Applicant has amended claim 6 so that it incorporates the limitations recited in claim 11, which specifies that the method comprises "treating said sample with a substance that cleaves the template nucleic acid without substantially cleaving the synthetic nucleic acid", " wherein said substance is a restriction enzyme".

For further clarification of Applicant's invention, the limitations recited in multiple dependent claims 7 and 11 through 18, as they apply to independent claim 6, have been transferred to newly added claims 19 through 25, by removing the dependency of multiple dependent claims 7 and 11 through 18, from independent claim 6. These limitations include a method comprising that "said synthetic nucleic acid is synthesized from said template", as required by Claim 7, that "said substance is a restriction enzyme", as required by claim 11, that "said restriction enzyme specifically cleaves nucleic acid comprising modified residues, without substantially cleaving un-modified residues", as required by Claim 12, that "said restriction enzyme specifically cleaves nucleic acid comprising un-modified residues, without substantially cleaving modified residues", as required by Claim 13, that "said restriction enzyme specifically cleaves double stranded nucleic acid, without substantially cleaving single stranded nucleic acid", as required by Claim 14, that "said template nucleic acid is a double stranded nucleic acid", as required by Claim 15, that "said synthetic nucleic acid is a single stranded nucleic acid", as required by Claim 16, that "said double-stranded template is produced in cells which incorporate methylated adenine residues into DNA molecules during replication", as required by Claim 17, and that "said cell is a dam+ E. coli cell", as required by Claim 18.

Because newly amended claim 6 recites a method comprising "a substance that cleaves the template nucleic acid and does not substantially cleave the RNA, wherein said substance is a

restriction enzyme", and since said method comprising a restriction enzyme is not taught by Carmichael et al., Applicant contends that Claim 6, dependent claim 9, and newly added dependent claims 19-25, are not anticipated by Carmichael et al.

Applicant also contends that because newly amended claim 1 and dependent claims 7-8 and 11-17 recite a method comprising a template and synthetic nucleic acid that comprise DNA, which is not taught by Carmichael et al., claims 1, 7-8 and 11-17 are not anticipated by Carmichael et al. Applicant further notes that claims 3, 5 and 10 have been canceled, as discussed previously. For the reasons described above, and in view of the claim amendments, reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections – 35 USC 103

Claims 1-17 are rejected under 103(a) as being unpatentable over McKernan et al (U.S. Serial No. 6,534,262) in view of Bauer et al. (U.S. Serial Number 5, 789,166).

Applicant traverses the rejection of claims 6-7 and 9 on the grounds that the cited references, whether considered in combination or individually, do not teach each and every recited claim limitation, specifically the limitation of "In a transcription reaction wherein a nucleic acid sample is generated comprising template nucleic acid and synthetic RNA" as recited in claims 6-7 and 9.

The Office Action describes the McKernan reference as teaching the removal of template DNA to ensure a high quality capillary sequencing product. The Office Action describes the Bauer et al. reference as teaching a conventional easy and effective method for removing template DNA by treating the sample with a restriction enzyme. However, neither reference teaches a method comprising "a transcription reaction wherein a nucleic acid sample is generated comprising template nucleic acid and synthetic RNA" as recited in claims 6-7 and 9.

The Office Action does state on page 4 that McKearnan et al teaches many molecular biology applications including reverse transcription. But reverse transcription comprises a template of RNA and synthetic DNA, which is not equivalent to the recited method comprising "template nucleic acid and synthetic RNA". Thus McKearnan does not teach the limitation of "In a transcription reaction wherein a nucleic acid sample is generated comprising template

nucleic acid and synthetic RNA" as recited in independent claim 6, and its dependent claims-7, 9 and newly added claims 19 through 26. Since Bauer et al. reference as teaching this limitation either, neither the McKearnan reference nor the Bauer reference teaches each and every limitation of claims 6-7 and 9, whether considered in combination or individually. Accordingly, withdrawal of this rejection is requested.

Solely for the purposes of advancing prosecution, claims 4-5 and 10 have been cancelled. As described previously, claim 1 has been amended so that it incorporates many of the analytical procedures recited in now canceled claim 3, but does not include the analytical procedures of DNA sequencing. Applicant notes that claim 3, which depended directly from claim 1, recited a method comprising an analytical procedure, "wherein said analytical procedure is selected from the group consisting of gel electrophoresis, anion-exchange chromatography, size-exclusion chromatography, pulse-field electrophoresis, polyacrylamide gel electrophoresis, sieving gel electrophoresis, Northern analysis, or Southern analysis". Applicant notes that neither McKernan et al. nor Bauer et al. individually teaches a method of preparing a nucleic acid sample for these specifically recited analytical procedures. Applicant contends that the Office Action does not address how the combination of these two references make obvious the method of newly amended Claim 1 and its dependent claims 1, 7-8 and 11-17, which comprise the following analytical procedures; gel electrophoresis, anion-exchange chromatography, size-exclusion chromatography, pulse-field electrophoresis, polyacrylamide gel electrophoresis, sieving gel electrophoresis, Northern analysis, or Southern analysis.

Applicant also traverses the rejection of Claim 17 on the grounds that the cited reference, when taken singly or when combined, do not present the limitation "wherein said the double stranded template is produced in cells which incorporate methylated adenine residues into DNA molecules during replication," required by Claim 17, because the references do not describe or discuss what cells the template was produced in. Since neither cited reference describes what cells the template was produced in, the cited references by McKearnan et al. and Bauer et al. can not be combined to make obvious the method recited in claim 17, which comprises the limitation that "the double stranded template is produced in cells which incorporate methylated adenine residues into DNA molecules during replication".

Claim 18 is rejected under 103(a) as being unpatentable in view of Bauer et al. (U.S. Serial Number 5, 789,166), as applied to claims 1-2, 5, 7-8 and 10-17 above, and further in view of McLeland et al. (U.S. Serial No. 4, 808,525).

The Applicant traverses the rejection of claim 18 on the grounds that the cited references, whether considered in combination or individually, do not teach each and every recited limitation of the claimed methods, specifically the limitation that "the double-stranded template is produced in dam+ *E. coli* cells".

The Office Action describes Bauer et al. as teaching a method for preparing a nucleic acid (from *E. coli*) for an analytical procedure, said method comprising treating said sample with a substance that cleaves the template nucleic acid without substantially cleaving said synthetic nucleic acid, but not teaching a method wherein the nucleic acid sample is obtained from dam+ *E. coli* cells. The Office Action further states that it would have been obvious to combine the teaching of McClelland that Dpn I cleaves DNA from Dam+ E. coli cells, with the teaching of Bauer et al. to arrive at the recited invention.

As described above, Applicant contends that Bauer et al. does not teach a method comprising subjecting said treated sample to one of the analytical procedures recited in newly amended claim 1, from which Claim 18 depends. As described previously, claim 1 has been amended so that it recites "A method of preparing a nucleic acid sample for an analytical procedure, said sample comprising template nucleic acid and synthetic nucleic acid, wherein said template and synthetic nucleic acid comprise DNA, said method comprising treating said sample with a substance that cleaves said template nucleic acid without substantially cleaving said synthetic nucleic acid, and subjecting said treated sample to an analytical procedure, wherein said analytical procedure is selected from the group consisting of gel electrophoresis, anion-exchange chromatography, size-exclusion chromatography, pulse-field electrophoresis, polyacrylamide gel electrophoresis, sieving gel electrophoresis, Northern analysis, or Southern analysis".

Further, Bauer et al. does not teach the method recited by Claim 1, comprising the further limitation "wherein said cell is a dam+ E. coli cell", as required by Claim 18, as part of a method which comprises preparing a nucleic acid sample for the recited analytical procedures

and subjecting said treated sample to an analytical procedure. Since McClelland's teaching that Dpn I cleaves DNA from dam+ E. coli cells does not makes up this omitted teaching in Bauer et al., Applicant contends the cited references, when taken either alone or in combination, do not make obvious Applicant's invention.

Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 18.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney/agent of record.

Respectfully submitted,

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